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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,507	11/05/2003	Ali Amara	03495.0301	6288

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/700,507	AMARA ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,10-12,24-34,36,40 and 81-115* is/are pending in the application.

4a) Of the above claim(s) *81-86 and 104-109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,10-12,24-34,36,40,87-103 and 110-115* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed July 26, 2005, is acknowledged and entered. Claims 2, 10-12, 24-34, 36, 40, 87-103 and 110-115 are under examination, being drawn to embodiments relating to treatment of viral diseases/inhibiting viral entry into cells, wherein the molecule that binds the DC-SIGN receptor is an effector molecule, specifically a viral glycoprotein or recombinantly produced protein. Please note that Groups II and IV are now rejoined with Group I. The restriction requirement between inventions I, II and IV is withdrawn. Upon further consideration, embodiments directed to methods using antibodies and recombinantly produced proteins are encompassed by the elected Group I. The method by which the effector molecules are produced (recombinantly) does not require further search.

The non-elected embodiment relating to treatment with mannosylated molecules (Group III, respectively) remains withdrawn from consideration, specifically claims 81-86 and 104-109.

Response to Amendment

2. The following objection and rejections are either moot or withdrawn:

- The objection to claims 1, 24 and 39 for failing to spell out the acronyms DC-SIGN, CMV and HIV at their first occurrence, respectively, is moot with regard to the cancellation of claims 24 and 39, and withdrawn with regard to the amended claim 24.
- The rejection of claims 24-30 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a cytomegalovirus (CMV) infection, does not reasonably provide enablement for preventing CMV infection, is

withdrawn in view of amended claims 24-30. Applicant's amendment to the claims specifies that the methods are for *treating* CMV infection.

- The rejection of claims 39, 40 and 42 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating human immunodeficiency virus (HIV) infection, does not reasonably provide enablement for preventing HIV infection, is moot in view of cancelled claims 39 and 42, and withdrawn in view of the amendment to claim 40. The amended claim 40 is drawn to *treatment* of HIV.
- The rejection of claims 1-3, 9-14, 24-30 and 39-42 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is moot with regard to cancelled claims 1, 3, 9, 13, 14, 39, 41 and 42, and withdrawn with regard to amended claims 2, 10-12, 24-30 and 40. The claims now recite endpoints that define the meaning of sufficient inhibition of binding.
- The rejection of claims 1, 2, 9-14, 39, 40 and 42 as provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 2, 9-14, 38, 39 and 41 of copending Application No. 10/700,491, is moot in view of the cancellation of those claims from the copending application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(*New rejection*) Claims 36, 102, 110 and 111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that monoclonal antibody Mab 1B10.2.6 from hybridoma cell 1B10.2.6 is required to practice the claimed invention because it is a necessary limitation for the success of the invention as stated in the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of Mab 1B10.2.6. See 37 CFR 1.802. One cannot practice the claimed invention without the antibody. One cannot determine whether an antibody has the necessary characteristics without access to Mab 1B10.2.6. Therefore, access to Mab 1B10.2.6 is required to practice the invention. The specification does not provide a repeatable method for Mab 1B10.2.6 without access to the Mab 1B10.2.6 and it does not appear to be readily available material.

Deposit of Mab 1B10.2.6 in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112., because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating

that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

4. Claims 2, 10-12, 24-34, 36, 40, 87-103 and 110-115 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims encompass the treatment of any disease, any viral disease, CMV and HIV, wherein a competitive inhibitor (effector molecule) inhibits binding of a pathogen to a DC-SIGN receptor. Clearly, Applicant has not demonstrated possession of a method that treats any disease, any viral disease, CMV or HIV. The specification does not put one of skill in possession of the large genus of methods claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a structure (effector molecule or binding moiety thereof) and a percent inhibition of binding to DC-SIGN. Applicant has not provided information of what structures must be present in order to result in 80% inhibition. In the case of HIV, the specification fails to demonstrate possession of a peptide that can cause 80% inhibition of binding to DC-SIGN. The specification fails to demonstrate which binding moiety of gp55 or what quantity is adequate to induce 80% inhibition. Accordingly, in the absence of sufficient recitation of distinguishing identifying

characteristics, the specification does not provide adequate written description of the claimed genus of methods.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

Claim Rejections - 35 USC § 102

5. Claims 2, 10, 87, 88, 113 and 114 are rejected under 35 U.S.C. 102(a) as being anticipated by Littman *et al.* (WO 01/64752 A2, "Littman"). (The claims are treated only with respect to the adequately described embodiments. References to 80% inhibition are not adequately described and are therefore not addressed in the rejection.) The claims as amended are drawn to a method of treating a disease of a mammal, wherein at least one symptom of the disease is mediated at least in part by the binding of an effector molecule to a DC-SIGN receptor

of the mammal to be treated. The method steps comprise administering to the mammal a molecule that specifically binds to the DC-SIGN receptor in an amount sufficient to inhibit the binding of the effector molecule to the DC-SIGN receptor by greater than 80% to thereby treat the disease of the mammal. Specifically, the disease being treated is a viral disease such as HIV, using a viral effector molecule. The molecules that bind to the DC-SIGN receptors can be antibodies that bind to HIV envelope 120.

Littman discloses antibodies (effector molecule) specific for the antigenic fragment of gp120 (envelope subunit protein of HIV and binding moiety of viral effector molecule) that inhibits DC-SIGN on dendritic cells from interacting with gp120. Also disclosed are methods of treating HIV infection by administering antibodies that bind to gp120, thereby inhibiting binding of gp120 to DC-SIGN. (See Littman, page 5, pages 5-6, bridging paragraph, and claims 1-4.) Therefore, Littman anticipates the claims.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the claims as amended require the effector molecule, in this case an antibody, to bind specifically to the DC-SIGN receptor. Applicant argues that Littman's antibodies are only disclosed as capable of binding gp120. Littman fails to teach that the antibodies specifically bind the DC-SIGN receptor.

In response to Applicant's arguments, any properties of Littman's antibodies are expected to be present regardless of whether those properties were or were not appreciated. In the instant case, Littman's antibodies are disclosed as capable of binding to gp120, thus inhibiting the interaction between gp120 on viruses with DC-SIGN receptors on dendritic cells. While Littman may not have appreciated the fact that gp120 antibodies can bind the DC-SIGN receptors on

dendritic cells, as Applicant did, the act of administering the antibodies is expected to result in the same effect: binding of DC-SIGN receptors. Littman administered the antibodies to the same patient population as Applicant. Therefore, the prior art anticipates Applicant's methods as claimed in claims 2, 10, 87, 88, 113 and 114.

6. Claims 2, 10, 87, 88, 113 and 114 are rejected under 35 U.S.C. 102(b) as being anticipated by Figdor *et al.* (EP 1046651 A1, "Figdor"). (The claims are treated only with respect to the adequately described embodiments. References to 80% inhibition are not adequately described and are therefore not addressed in the rejection.) The claims are summarized above.

Figdor discloses a method for treating HIV infection in humans comprising administering humanized monoclonal antibodies (effector molecules) that bind DC-SIGN receptors on dendritic cells. The binding of DC-SIGN prevents HIV gp120 (binding moiety of viral effector molecule) from interacting with DC-SIGN (page 4, [0040], page 5, [0046] and page 7, [0070]-[0071]). Therefore, the claims are anticipated by Figdor.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the claims as amended require that the effector molecule, in this case an antibody, comprise a binding moiety that specifically binds to the DC-SIGN receptor. Applicant argues that Figdor's antibodies do not contain a binding moiety that specifically binds to the DC-SIGN receptor.

In response to Applicant's arguments, any properties of Figdor's antibodies are expected to be present regardless of whether those properties were or were not appreciated. In the instant

case, Figdor's antibodies are disclosed as capable of binding to gp120, thus inhibiting the interaction between gp120 on viruses with DC-SIGN receptors on dendritic cells. While Figdor may not have appreciated the fact that gp120 antibodies can bind the DC-SIGN receptors on dendritic cells, as Applicant did, the act of administering the antibodies is expected to result in the same effect: binding of DC-SIGN receptors. Figdor administered the antibodies to the same patient population as Applicant. Therefore, the prior art anticipates Applicant's methods as claimed in claims 2, 10, 87, 88, 113 and 114.

7. Claims 2, 10-12, 24-34, 36, 40, 87-103, 110-115 are rejected under 35 U.S.C. 102(b) as being anticipated by Gehrz *et al.* (WO 91/05876, herein, "Gehrz"). (The claims are treated only with respect to the adequately described embodiments. References to 80% inhibition are not adequately described and are therefore not addressed in the rejection.) The claims are summarized above. Specifically, the disease being treated is a viral disease, such as cytomegalovirus (CMV) wherein the viral effector molecule is a molecular constituent of the viral envelope, such as envelope glycoprotein B. The claimed method can also treat HIV disease/infection in a human using the CMV glycoprotein B blocking derivative.

Gehrz discloses a method for treating human CMV with a cocktail of monoclonal antibodies, one of which binds to gp55, a subunit of envelope glycoprotein B (abstract and Example 1). The method can be practiced on human patients with HCMV infections, including those with acquired immune deficiency (AIDS). The antibodies include humanized antibodies (page 36-37, bridging paragraph). Antibodies to gp55 are binding moieties and constituents themselves. Although Gehrz does not mention that the monoclonal antibodies bind to DC-SIGN

to interrupt binding between glycoprotein B and DC-SIGN, Gehrz's antibodies are inherently interacting with DC-SIGN. When Gehrz administers the antibody cocktail to an AIDS patient (infected with HIV), the antibody cocktail is inherently acting on DC-SIGN. Regarding the limitation of recombinantly produced proteins, the monoclonal antibodies of the Gehrz are recombinantly produced. Therefore, the claims are anticipated by Gehrz.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's arguments are primarily directed to the following:

- Applicant argues that the claims as amended require a molecule that specifically binds to the DC-SIGN receptor. Gehrz's monoclonal antibodies are disclosed as binding to CMV proteins. Applicant argues that the DC-SIGN receptor is not a CMV protein.
    - In response to Applicant's arguments, the Office recognizes that the DC-SIGN receptor is not a CMV protein. However, the interaction between Gehrz's antibodies and DC-SIGN is expected to take place because the antibodies are effector molecules. The instant claims only require that the molecular effector be an antibody.
- Applicant argues that even if Gehrz's antibodies are inherently interacting with DC-SIGN by binding to CMV, thus restricting the interaction between DC-SIGN and CMV, the claimed method uses a molecule that specifically binds to the DC-SIGN receptor.
    - In response to Applicant's arguments, the antibodies of Gehrz are expected to bind to DC-SIGN because they meet the structural

requirements outlined in the claims. The functions of the antibodies are expected to be the same as those described by Applicant, lacking evidence to the contrary.

In summary, the activity of the prior art's antibody is expected to be the same as those antibodies instantly claimed. While Gehrz did not appreciate certain activities or capabilities of the antibodies, the activities and capabilities inherent in the antibodies are present regardless. In this case, the patient population is the same as Applicant's intended patient population. Therefore, administering Gehrz's antibodies, which are considered to be the same as Applicant's antibodies, would necessarily result in the binding of DC-SIGN.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 10-12, 87, 88, 113 and 114 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-34, 78-89 and 96-100 of copending Application No. 10/700,491. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are a

genus of the copending claimed species. The instant claims are drawn to methods of treating viral infection (generically) and inhibiting viral entry of cells (generically). The claims of the copending application are drawn to treating Flavivirus infection and inhibiting flavivirus entry of cells. The copending claims are species of the instant genus claims. Species claims obviate genus claims. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

9. No claim is allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen
October 13, 2005